REMARKS

This amendment is in response to the final office action mailed July 17, 2007, in which the Patent Office rejected claims 1-12, all of the claims then pending. Applicants hereby submit amendments to claims 1, 5 and 6, and new claims 14-18. These amendments are believed to place the claims in form for allowance, or in better form for appeal. New claims 14-18 are believed to be free of the pending rejections. No new matter is added by these amendments. Entry of the present amendments, and reconsideration and withdrawal of the pending rejections, are respectfully requested.

Claim objections

The Patent Office has objected to claims 5 and 6 under 37 CFR 1.75(c), as being of improper dependent form. Office Action, page 2. Specifically, the Patent Office stated that

> [t]he recitations in claims 5 and 6 "or a derivative thereof having the autoproteolytic activity of the autoprotease N^{PRO} of classic swine fever virus", remove any distinction between polynucleotides of these claims and a polynucleotide of claim 1 encoding the amino acid sequence of a generic pestivirus autoprotease N^{PRO} where claims 5 and 6 fail to otherwise indicate any functional or structural difference between an autoproteolytic activity of a classic swine fever virus autoprotease N^{PRO} and the autoproteolytic activity of a generic pestivirus autoprotease N^{PRO}, and no such distinction is disclosed in the specification.

Id.

The recitation "or a derivative thereof having the autoproteolytic activity of the autoprotease N^{pro} of classic swine fever virus" has been removed from claims 5 and 6 (as well as in claim 1) by the present amendment. As presently amended, claims 5 and 6 recite specific structural distinctions that further limit the subject matter of claim 1, from which they depend. Withdrawal of the claim objections is therefore proper, and respectfully requested.

Rejections under 35 USC § 112, first paragraph (written description)

The Patent Office has rejected claims 1-12 under 35 USC § 112, first paragraph as lacking adequate written description in the specification. Specifically, the Patent Office stated that

> ... the specification fails to exemplify or describe the preparation of divergent pestivirus N^{PRO} proteases that far exceed deletions of the amino-proximal regions recited in claims 5 and 6 and exceed the introduction of one or few amino acid substitutions because they reach derivatives that need have no particular, or very limited, structural relationship to the amino acid sequence set forth in SEQ ID NO: 1. ... The rejection of record is sustained because the

> specification's treatment of "derivatives" of pestivirus N^{PRO} autoproteases is entirely prospective.

Office Action, page 3.

The phrase "or a derivative thereof ... autoprotease N^{pro}" claims 1, 5 and 6 has been removed by the present amendments. The claims as presently amended are directed to subject matter that is specifically described in the specification at, *inter alia*, pages 6-7 and in Examples 1 and 2. Therefore, the applicants believe that these amendments overcome this rejection, and place the claims in form for allowance. New claims 14-18 have been added, which are directed to specific derivatives of the N^{pro} autoprotease of classic swine fever virus (the sequence of which is set out in SEQ ID NO: 1).

New claim 14 recites a nucleic acid molecule of claim 1, wherein the first polypeptide consists of an amino acid sequence SEQ ID NO. 1 in which one or more of amino acids 2-21 have been deleted or substituted. Support for claim 14 is found, *inter alia*, at page 6 of the specification, which states that

> [a] preferred autoprotease N^{pro} derivative of the described fusion protein has, for example, an N-terminal region in which one or more amino acids have been deleted or substituted in the region of amino acids 2 to 21 as long as the resulting derivative continues to exhibit the autoproteolytic function of the autoprotease N^{pro} to the desired extent.

Further support for claim 14 is found in Examples 1 and 2 (first 16 amino acids of the natural N^{pro} sequence replaced by a peptide consisting of 10 histidines).

New claim 15 recites a nucleic acid molecule according to claim 14, wherein the first polypeptide consists of the amino acid sequence of SEQ ID NO: 1 in which amino acids 2-16 have been deleted. Support for claim 15 is found, *inter alia*, at page 6 as quoted above, which additionally states that

> [i]n the context of the present invention, autoprotease N^{pro} derivatives which are preferred in the fusion protein comprise, for example, the amino acid sequence of the autoprotease N^{pro} of CSFV with a deletion of amino acids 2 to 16 or 2 to 21.

Further support for claim 15 is found in the specification at page 7, first full paragraph, and in original claim 6.

New claim 16 recites a nucleic acid molecule of claim 15, wherein the first polypeptide consists of the amino acid sequence of SEQ ID NO: 1 in which amino acids 2-21 have been deleted. Support for claim 16 is found, *inter alia*, in the specification at page 6 as quoted above, and in the paragraph bridging pages 6 and 7, which states that

> [a] particularly preferred molecule according to the present invention is one where the first polypeptide comprises the amino

> acid sequence Glu22 to Cys168 of the autoprotease N^{pro} of CSFV ... the first polypeptide furthermore having a Met as N-terminus ...

Further support is found in original claim 5.

New claim 17 recites a nucleic acid molecule coding for a fusion protein comprising a first nucleic acid sequence encoding a first polypeptide consisting of an amino acid sequence corresponding to Glu22 to Cys168 of SEQ ID NO. 1 and having a Met as the N-terminus, and a second nucleic acid sequence encoding a second polypeptide which is heterologous with respect to the first polypeptide and is directly covalently bound to the C-terminus of the first polypeptide in a manner such that the second polypeptide is capable of being cleaved from the fusion protein by the autoproteolytic activity of the first polypeptide. Support for claim 17 is found in the specification at, *inter alia*, pages 6 and 7 as quoted above, and in original claim 5.

New claim 18 recites a nucleic acid molecule of claim 14, wherein amino acids 2-16 are replaced by a polypeptide consisting of 10 histadines. Support for claim 18 is found in the specification at, *inter alia*, page 6 as quoted above, and in Examples 1 and 2 (first 16 amino acids of the natural N^{pro} sequence replaces by a peptide consisting of 10 histidines).

The forgoing establishes that each of claims 1-12 and 14-18 have specific, express written description support in the specification, and that no new matter is added by new claims 14-18. Entry of the present amendments, and reconsideration and withdrawal of this rejection are respectfully requested.

Rejections under 35 USC § 112, first paragraph (enablement)

The Patent Office has rejected claims 1-12 under 35 USC § 112, first paragraph, as lacking an enabling disclosure in the specification. Specifically, the Patent Office stated that

> claims 1, 5, and 6, and claims 2-4 and 7-12 that depend therefrom, contemplate an arbitrary number of amino acid substitutions, additions or deletions anywhere within pestivirus N^{PRO} autoprotease amino acid sequences, including modification occurring even with the core functional region corresponding to the sequence of amino acids from position 22 through position 168 of SEQ ID NO: 1. See the discussion at pages 5 and 6 of the specification, Even if combined with the teachings of the prior art made of record herein the specification cannot support the introduction of an unspecified number of amino acid sequence alterations in the core, functional, region of a pestivirus N^{PRO} autoprotease amino acid sequence, in any combination or any pattern.

Office Action, page 4.

By the present amendment the reference to "derivatives" has been removed from claims 1, 5 and 6. As presently amended, claim 1 no longer recites what the Patent Office refers to as

"an arbitrary number of amino acid substitutions, additions or deletions anywhere within pestivirus N^{PRO} autoprotease amino acid sequences." Applicants believe that as presently amended claim 1 is fully enabled by the disclosure throughout the specification. As presently amended, claims 5 and 6 recite specific alterations to the sequence of the autoprotease N^{pro} of CSFV. Enabling support for claims 5 and 6 as presently amended is found throughout the specification, in particular at pages 5-7 and in Examples 1 and 2. The rejection of dependent claims 2-4 and 7-12 was based on the asserted lack of enablement of then-pending claims 1, 5, and 6. As claims 1, 5, and 6, as presently amended, are fully enabled by the specification, withdrawal of the rejection of claims 2-4 and 7-12 is proper.

New claims 14-18 all recite well-defined nucleic acid sequences, which also find enabling disclosure throughout the specification, in particular at pages 5-7 and in Examples 1 and 2. Applicants submit that the present rejection for lack of enablement is not applicable to new claims 14-18. Entry of the present amendments, and reconsideration and withdrawal of this rejection, are respectfully requested.

Rejections under 35 USC § 112, second paragraph

The Patent Office has rejected claims 1-12 under 35 USC § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the applicants' invention. Office Action, page 5. Specifically, the Patent Office stated that the term "derivative thereof with autoproteolytic activity" recited in claims 1, 5, and 6 was indefinite because

> [t]hese phrases indicate no characteristic other than autoproteolysis and the artisan and the public seeking to determine the metes and bounds of the intended subject matter cannot ascertain the structure of any derivatives from the specification's disclosure, particularly where the recitations, "having the autoproteolytic activity of the autoprotease N^{PRO} of classic swine fever virus", in claims 5 and 6 permit the replacement of the amino-terminal amino acids indicated as deleted with part or all of the regions removed, or with an unrelated amino acid sequence.

Office Action, page 5. The Patent Office indicated that this rejection "may overcome by deleting the phrases that necessitate this rejection of claims 1, 5, and 6 and claims 2-4 and 7-12 that depend therefrom." *Id.*

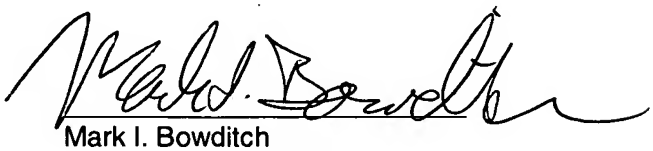
The applicants take the Patent Office's reference to "the phrases that necessitate this rejection of claims 1, 5, and 6" to mean the recitation in those claims of "a derivative thereof having autoproteolytic activity." As suggested by the Patent Office, the present amendments remove this reference to "derivatives." The applicants therefore believe that the present amendments overcome this rejection of claims 1-12. Furthermore, new claims 14-18 do not recite "a derivative thereof having autoproteolytic activity," or similar language, and therefore the

applicants submit that this rejection is not applicable to new claims 14-18. Entry of the present amendments, and reconsideration and withdrawal of this rejection, are respectfully requested.

CONCLUSION

In view of the present amendments to the claims, and the foregoing remarks, the applicants believe that pending claims 1-12, as presently amended, and new claims 14-18, are in full compliance with the requires of 35 USC § 112, first and second paragraphs, and are therefore in condition for allowance. Entry of the present amendments, and reconsideration and withdrawal the pending rejections, are respectfully requested. Favorable action on the claims is earnestly solicited.

Respectfully submitted,



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Date: January 17, 2008